Therapeutic paralysis

March 30, 2025 by **Josh Farkas**

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aminosteroid paralytics (rocuronium, vecuronium)

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contraindications, drug interactions, side effects 👎

contraindications

- Allergic reaction history.

drug-drug interactions

- Potentiation of neuromuscular blockade:
  - Antibiotics (aminoglycosides, tetracyclines, vancomycin, clindamycin, colistin).
  - Magnesium, lithium.
  - Lidocaine (when administered systemically); other local anesthetics.
  - Quinidine, procainamide.
  - Dantrolene.
- Chronic anticonvulsant therapy (e.g., phenytoin, carbamazepine, valproic acid, possibly levetiracetam) may lead to resistance due to upregulation of acetylcholine receptors.
- Succinylcholine may block or augment paralysis.
- (There are no pharmacokinetic drug-drug interactions. Pharmacodynamic reactions are the same between both rocuronium and vecuronium.)

side effects

- Allergic reactions (more common in some countries than others due to the prevalence of cross-allergenic substances in the environment; less common in the United States).
- Prolonged/residual paralysis (discussed further below in the pharmacokinetics section).
- Myopathy (primarily with ongoing infusion, rather than a single dose).

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indications, advantages 👍

- Rocurinum is the drug of choice for intubation among critically ill patients.
- Vecuronium is commonly utilized among intubated patients to cause short-term paralysis.
- Aminosteroid paralytics (rocuronium, vecuronium) aren't ideal for maintenance infusions due to the increased risk of myopathy and drug accumulation. Cisatracurium is the preferred agent for ongoing paralytic infusions (discussed below).

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dosing

ROCuronium dosing

- **Initial induction dose for RSI**:
  - For critical care RSI a reasonable dose is 1.2 mg/kg. (34178382 (https://pubmed.ncbi.nlm.nih.gov/34178382/)) However, some limited evidence does support the use of higher doses of rocuronium (≧ 1.4 mg/kg). Higher doses may be reasonable in patients with shock who may experience a delayed onset of paralysis. If higher doses are used, practitioners must expect and plan for a prolonged duration of paralysis. (33837951 (https://pubmed.ncbi.nlm.nih.gov/33837951/))
  - For elective anesthesia, lower doses are often used (e.g., 0.6-1 mg/kg). This may facilitate more rapid weaning off the ventilator.
  - Onset of paralysis: 1-2 minutes (shorter with higher dose).
- **Continuous infusion**:
  - Start infusion at ~10 ug/kg/min (0.6 mg/kg/hour).
  - Titrate over a range of ~4-16 ug/kg/min (0.25-1 mg/kg/hour).
  - The dose requirement often drops by 40% after 6-9 hours (tissue redistribution accounts for 80% of initial metabolism). (27842752 (https://pubmed.ncbi.nlm.nih.gov/27842752/) , Irwin & Rippe 9e)
  - Ideally, infuse centrally since it's acidic. (Paw & Shulman 2025)

VECuronium dosing

- **Initial loading dose**:
  - A typical dose is 0.1 mg/kg (or a flat dose of 10 mg).

    - The onset of paralysis occurs over 3-4 minutes (making this a *poor* choice for RSI).
- **Continuous infusion**:
    - Start at 1 ug/kg/min (0.06 mg/kg/hour).
    - Titrate over a range of ~0.8-2.3 ug/kg/min (0.05-0.14 mg/kg/hour). (27842752 (https://pubmed.ncbi.nlm.nih.gov/27842752/))

dosing aminosteroid paralytics in morbid obesity

- Dosing may be based on lean body weight. Lean body weight rarely exceeds 70 kg in women or 100 kg in men. (25950621 (https://pubmed.ncbi.nlm.nih.gov/25950621/))
    - 150 mg of rocuronium should be sufficient.
    - Lean body weight calculator: 🧮 (https://evidencio.com/models/show/519)

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pharmacology

ROCuronium pharmacology

- **Chemical properties**:
    - Molecular weight: 610 g/mol.
    - LogP: 0.5
- **Absorption**:
    - IV/IO administration.
- **Distribution**:
    - Protein binding is 30%.
    - Vd is 0.22 L/kg.
- **Metabolism**:
    - Minimal hepatic *metabolism*.
- **Elimination**:
    - ~70% occurs mostly via hepatic uptake and biliary excretion. Hepatic uptake transporters include MATE1, OCT1, OATP1B1, and OATP1B3. Hepatic dysfunction causes a moderate delay in excretion.
    - ~30% is excreted in the urine. Renal dysfunction causes minimal effect on kinetics.
- **Half-life & duration of action**:
    - Half-life: ~1.4-2.4 hours.

    - Time to recovery: ~60-70 minutes (but may vary due to several factors as discussed immediately below).
    - Recovery time may partially reflect drug *redistribution*.
- **Risk factors for prolonged paralysis from rocuronium**:
    - [1] Larger doses of rocuronium:
        - 1.2 mg/kg vs. 0.6 mg/kg.
        - Dosing an obese patient based on actual body weight.
    - [2] Hepatic dysfunction > renal dysfunction.
    - [3] Older age.
    - [4] Other drugs that may potentiate paralysis (listed above under *drug-drug interactions*).
    - ⚠️ The duration of paralysis can be *fickle.* Some patients may experience prolonged paralysis without wholly obvious reasons. Don't assume that the half-life of rocuronium is the same for every individual patient.

VECuronium pharmacology

- **Chemical properties**:
    - Molecular weight: 637 g/mol.
    - LogP: 0.75 (slightly more lipophilic than rocuronium).
- **Absorption**:
    - IV administration.
- **Distribution**:
    - Protein binding is ~70%.
    - The Vd is ~0.3-0.4 L/kg (larger than for rocuronium).
- **Metabolism**:
    - ~20-30% is metabolized by the liver via deacetylation, yielding active metabolites. 3-diacetyl-vecuronium is the primary metabolite, with 50-80% of the potency of vecuronium. Renal failure may cause accumulation of the metabolite over time with repeated administration or continuous infusion. When vecuronium is given as a single dose, serum levels of 3-diacetyl-vecuronium are generally negligible.
- **Elimination**:
    - ~35% excreted in the urine unchanged.
    - ~25-50% excreted in the bile.
- **Half-life & duration of action are *shorter* than rocuronium**:

- Half-life:
  - Healthy adults: ~60 minutes.
  - Cirrhosis or elderly: ~90 minutes.
  - Late pregnancy: ~40 minutes.
- Time until recovery: ~45-60 minutes.

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cisatracurium

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contraindications, drug interactions, side effects 👎

contraindications

- Hypersensitivity to cisatracurium.

drug-drug interactions

- Potentiation of neuromuscular blockade:
  - Antibiotics (aminoglycosides, tetracyclines, vancomycin, clindamycin, colistin).
  - Magnesium, lithium.
  - Lidocaine (when administered systemically); other local anesthetics.
  - Quinidine, procainamide.
  - Dantrolene.
- Chronic anticonvulsant therapy (e.g., phenytoin, carbamazepine, valproic acid, possibly levetiracetam) may lead to resistance due to upregulation of acetylcholine receptors.
- Succinylcholine may block or augment paralysis.

side effects

- Anaphylaxis or anaphylactoid reactions (including bronchospasm).
- Bradycardia (0.4%), hypotension (0.2%).
- CNS toxicity may rarely result from accumulation of laudanosine metabolite (e.g., seizures), but this is rare with standard dosing.

indications, advantages 👍

- Cisatracurium is generally the preferred paralytic infusion of choice.
  - Its metabolism is more reliable, avoiding accumulation (especially in patients with renal and/or hepatic dysfunction).
  - Cisatracurium may cause fewer neuromuscular side effects than aminosteroid paralytics. (23062076 (https://www.ncbi.nlm.nih.gov/pubmed/23062076))
- Cisatracurium is an enantiomerically purified version of atracurium (which is a racemic mixture). As such, cisatracurium is generally preferable to atracurium.

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dosing

- **Initial dose**:
  - Cisatracurium: 0.1-0.2 mg/kg
    - 0.1 mg/kg loading dose for ventilator synchrony.
    - 0.2 mg/kg may be used for RSI.
  - Onset in 2-3 minutes.
- **Infusion dose**:
  - Start at 3 mcg/kg/min.
  - Titrate in the range of ~0.5-10 mcg/kg/min. (27842752 (https://pubmed.ncbi.nlm.nih.gov/27842752/)) Typically titrate by one mcg/kg/min every two hours.
  - ACURASYS used a fixed 15 mg bolus followed by a 37.5 mg/hr infusion (625 mcg/min, which is ~9 mcg/kg/min). This isn't recommended but rather is intended merely to provide some context.

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pharmacology

- **Chemical properties**:
  - Molecular weight: 929 g/mol.
  - LogP: -2.2

- **Absorption**:
  - IV administration.
- **Distribution**:
  - Protein binding is unknown (the drug disintegrates too fast to test this accurately).
  - Vd is small (0.15 L/kg). Given the molecule's size and hydrophilicity, it distributes into the extracellular fluid.
- **Metabolism**:
  - Metabolism is via Hoffman elimination:
    - Not significantly affected by renal/hepatic organ function.
    - It does depend on pH and temperature.
  - Active metabolites: Laudanosine (less so with cisatracurium; probably not clinically relevant; renally excreted).
- **Elimination**:
  - Metabolites are primarily eliminated through the urine (95%).
- **Half-life & duration of action**:
  - The half-life is 22-31 minutes, with low inter-patient variability.
  - Recovery may occur after ~60-90 minutes (range 20-270 minutes). (27842752 (https://pubmed.ncbi.nlm.nih.gov/27842752/))
  - Clearance may be prolonged due to hypothermia and acidosis since Hofmann elimination depends on pH and temperature.

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succinylcholine

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contraindications, drug interactions, side effects 👎

contraindications

- Malignant hyperthermia (personal or family history).
- Myasthenia gravis (resistance to succinylcholine).
- Bradycardia (relative contraindication; succinylcholine may rarely cause bradycardia).
- Hyperkalemia:

    - On average, expect a 0.5-1 mM rise. However, patients with conditions listed below may experience exaggerated elevations of potassium. (Paw & Shulman 2025)
- Major burns or crush injuries.
- Immobilization >14 days; critical illness myopathy. (Wellington 3e)
- Neuromuscular disorders causing denervation for >2 days or skeletal myopathies, including:
    - Stroke, encephalitis, amyotrophic lateral sclerosis.
    - Spinal cord disease.
    - Neuropathies (e.g., Guillain-Barré syndrome).
    - Muscular dystrophies.
- Penetrating eye injury (may increase intraocular pressure).

drug-drug interactions

- Some drugs may potentiate the neuromuscular blockade, but this is generally not a problem.
- Some drugs may reduce pseudocholinesterase levels, potentially leading to prolonged paralysis (discussed further below in the section on pharmacokinetics).

side effects

- [1] Hyperkalemia. This effect is usually moderate but may be more pronounced among patients who experienced denervation, leading to increased sensitivity to acetylcholine.
- [2] Malignant hyperthermia:
    - Usually occurs shortly after administration (e.g., <1 hour).
    - Initial features may include tachycardia, cyanosis, and muscle rigidity (especially the *masseter*).
    - Further discussion of malignant hyperthermia: 📖 (https://emcrit.org/ibcc/mh/#top)
- [3] Bradycardia rarely occurs due to increased vagal activity. Some authors advocate routine administration of atropine or glycopyrrolate to avoid bradycardia. (Paw & Shulman 2025)
- [4] Prolonged paralysis due to pseudocholinesterase deficiency. This may be genetic, or it may be associated with malnutrition, liver disease, uremia, pregnancy, burns, plasmapheresis, or oral contraceptives.
- [5] Transient increase in intracranial pressure and intraocular pressure.

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indications, advantages 👍

- The primary advantage of succinylcholine is its short duration of activity, which may facilitate subsequent neurological examination or extubation. However, with the development of sugammadex, this is less important.
- Succinylcholine is suboptimal for routine ICU intubations because there are numerous contraindications (listed above), many of which are common among critically ill patients and easily overlooked.

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succinylcholine dosing for RSI

- **Intravenous administration**:
  - The dose is 1-1.5 mg/kg (repeat dose of 0.5 mg/kg can be given PRN). (Paw & Shulman 2025)
  - Onset of action is ~45 seconds.
  - Waiting 30 seconds after the onset of fasciculation should provide optimal timing for intubation. (32483489 (https://pubmed.ncbi.nlm.nih.gov/32483489/))
- **Intramuscular**:
  - Dose is 3-4 mg/kg IM.
  - Paralysis usually occurs after 2-3 minutes.
  - ⚠️ This isn't preferred. Establishing an IO access may often be safer if additional medications are required after intubation.
- Morbid obesity: based on actual weight (plasma cholinesterase activity is increased in obesity). (34178382 (https://pubmed.ncbi.nlm.nih.gov/34178382/))

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pharmacology

- **Chemical properties**:
  - Molecular weight: 361 g/mol.
  - LogP: -4.2
- **Absorption**:
  - IV is obviously preferred.
  - IM can be utilized for RSI (dose above).
- **Distribution**:

    - Vd is very low (succinylcholine is highly ionized with a LogP of -4.2).
    - Doesn't cross the blood-brain barrier.
- **Metabolism**:
    - Rapidly hydrolyzed by plasma pseudocholinesterase (aka butyrylcholinesterase) to succinylmonocholine (which has minimal activity).
- **Elimination**:
    - ~10% is excreted unchanged in the urine.
- **Half-life & duration of action**:
    - The mean half-life is ~47 seconds. Plasma levels usually fall to undetectable levels within 2.5 minutes after an IV bolus of 1-2 mg/kg. The duration of neuromuscular blockade may last ~4-6 minutes.
    - Genetic or acquired deficiencies in pseudocholinesterase may markedly prolong paralysis.
        - Liver failure (pseudocholinesterase is synthesized in the liver).
        - Genetic pseudocholinesterase deficiency.
        - Some medications reduce pseudocholinesterase activity (e.g., oral contraceptives, glucocorticoids, pyridostigmine, physostigmine, rivastigmine, neostigmine, some monoamine oxidase inhibitors, organophosphate insecticides).

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indications for paralysis

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paralysis to promote ventilator synchrony

potential benefits

- Paralysis reduces metabolic activity, which reduces CO2 production and O2 consumption. This could help slightly in patients with severely impaired gas exchange.
- Complete avoidance of ventilator dyssynchrony, which may help limit peak pressures and reduce the risk of barotrauma (e.g., pneumothorax).
- May facilitate prone positioning (although paralysis is not mandatory for prone patients).
- May promote accurate measurement of plateau pressures.

potential risks

- Listed below: ⚡ (#otherrisks)

data regarding paralysis in ARDS

- The ACURASYS trial in France evaluated early paralysis with cisatracurium for 48 hours among patients with PaO2/FiO2 <150 mm. The study purported to show a mortality benefit, but this was only statistically significant within an adjusted analysis (*not* based on the raw data). (20843245 (https://pubmed.ncbi.nlm.nih.gov/20843245/))
- The larger ROSE 🌹 multi-center RCT subsequently found *no benefit* from routine cisatracurium paralysis (compared with a strategy of as-needed paralysis, which resulted in 15% of patients in the control arm receiving paralytic). (31112383 (https://pubmed.ncbi.nlm.nih.gov/31112383/)) There was an increased rate of cardiovascular events among patients treated with paralysis. (31433931 (https://pubmed.ncbi.nlm.nih.gov/31433931/))
- Considering the totality of evidence, it's likely that routine paralysis *never* improved mortality (as implied by the adjusted results of the ACURASYS trial).
- Meta-analyses have shown that paralysis *is* associated with improvement in *oxygenation*. (32483489 (https://pubmed.ncbi.nlm.nih.gov/32483489/))

summary of evidence-based medicine on paralysis to promote ventilator synchrony

- Routine application of paralysis doesn't improve mortality in ARDS.
- Indications for paralysis may include:
  - Refractory hypoxemia.
  - Persistent ventilator dysynchrony posing a threat to lung-protective ventilation that is refractory to other interventions (further discussion of therapies that can be deployed to avoid paralysis below: ⚡ (#management_of_ventilator_dyssynchrony_&_how_to_avoid_a_paralytic_infusion_for_ventilator_synchrony)).
- Cisatracurim is arguably the preferred agent:
  - Cisatracurium is supported by a greater evidentiary basis in terms of safety (e.g., ACURASYS and ROSE trials).
  - Cisatracurim likely produces a reduced risk of ICU-related weakness than aminosteroid paralytics.

- If a paralytic is used, the lowest possible dose should be utilized for the shortest possible duration of time. This hasn't been proven in a rigorous, prospective fashion, but there is data correlating the duration of paralysis with escalating risk.

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other indications for paralysis

hyperthermia

- Paralysis will immediately shut down all thermal energy generation from muscles.
- Short-term paralysis may be required to treat hyperthermia due to various intoxications (e.g., serotonin syndrome).

shivering

- Paralysis is a treatment of *last resort* for managing shivering (e.g., in the context of therapeutic temperature monitoring status post-cardiac arrest).
- Before paralysis, a multimodal package of shivering-suppressive therapies should be instituted as described here: 📖 (https://emcrit.org/ibcc/post-arrest/#shivering_management)

abdominal compartment syndrome or ICP elevation

- Rarely, paralysis may be required to prevent pressure fluctuations caused by coughing or bucking the ventilator.

refractory shock

- Rarely, it may be desirable to eliminate the work of breathing entirely. Paralysis will reduce blood flow to the diaphragm, allowing it to be shunted to vital organs.
- Note, however, that eliminating the respiratory drive with *deep sedation* may similarly reduce the work of breathing.

procedures or MRI scanning (short-term paralysis)

- Short-term paralysis may improve the safety of delicate procedures.
- Paralysis is often desirable before MRI scanning to obtain a high-quality scan and avoid self-extubation in the MRI (patients can tongue out the tube, even if their hands are restrained).

management of ventilator dyssynchrony & how to avoid a paralytic infusion for ventilator synchrony

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The most common indication for a paralytic infusion in the ICU is the management of ventilator dyssynchrony. Paralysis will make patients look beautiful but carries substantial risks (as outlined below ⚡ (#otherrisks)). Consequently, paralysis should be avoided when possible (especially in asthmatic patients, who may be at increased risk of myopathy). Below are several strategies to avoid paralysis when able, which, as always, must be tailored to any specific patient. It's usually possible to sedate the patient enough that they're passive on the ventilator – in which case, it's doubtful that adding a paralytic will cause clinical benefit.

[1/6] adjust the ventilator to improve patient comfort

- The classic adage is "fit the ventilator to the patient, don't fit the patient to the ventilator."
- Maximal efforts should always be made to improve patient comfort by adjusting the ventilator before instituting chemical paralysis. For example:
  - If there is evidence of flow-starvation in volume-cycled ventilation modes, the flow rate may be increased. Alternatively, switching to pressure-support ventilator modes may often improve patient comfort.
  - Small increases in tidal volume (e.g., from 6 cc/kg to 8 cc/kg) may improve dyssynchrony. (33381233 (https://pubmed.ncbi.nlm.nih.gov/33381233/))

[2/6] permissive hypercapnia

- Most patients will tolerate hypercapnia very well (in the absence of right ventricular failure).
- IV bicarbonate may help improve the pH and allay concerns about acidemia (discussed further below).
- pH and pCO2 targets are wholly arbitrary, so instituting a paralytic infusion due to failure to meet some arbitrary threshold is usually misguided (e.g., "the pH was below 7.15 so we needed to paralyze the patient").

[3/6] suppress the respiratory drive

- *Respiratory drive suppression is the single most potent approach to avoiding paralysis. This may be achieved with a multi-modal combination of several interventions.*
- Medications:
  - [1] Opioids.
  - [2] Propofol.
    - Propofol blunts the respiratory drive.
    - Propofol may reduce oxygen consumption and CO2 production. (27842752 (https://pubmed.ncbi.nlm.nih.gov/27842752/))
  - [3] Benzodiazepines, when combined with opioids (when given alone, benzodiazepines have little effect on respiratory drive). (27842752 (https://pubmed.ncbi.nlm.nih.gov/27842752/))
  - [4] IV bicarbonate +/- loop diuretics to improve the serum bicarbonate (thereby reducing the respiratory drive). (5933194 (https://pubmed.ncbi.nlm.nih.gov/5933194/), 8718911 (https://pubmed.ncbi.nlm.nih.gov/8718911/), 16695940 (https://pubmed.ncbi.nlm.nih.gov/16695940/), 889648 (https://pubmed.ncbi.nlm.nih.gov/889648/), 29307724 (https://pubmed.ncbi.nlm.nih.gov/29307724/)) Remember that metabolic acidosis will *increase* the respiratory drive (in an effort to mount a compensatory respiratory alkalosis), making the patient feel more air-hungry.
  - [5] Phenobarbital. 💉 (https://emcrit.org/ibcc/sz/#phenobarbital)
- Reduce endogenous CO2 production (e.g., temperature control, treatment of agitation).

[4/6] it's OK if the patient doesn't *look* perfect

- Paralysis will make patients *appear peaceful*, but paralysis doesn't necessarily improve the *patient's experience* of mechanical ventilation (in fact, paralysis may make their experience infinitely worse by creating a risk of *awareness while paralyzed*).
- We need to be mindful of precisely what we are aiming for here: our *perception* of the patient's comfort versus the patient's *actual* comfort.
- Some patients may *look bad* during mechanical ventilation (e.g., with retractions or a shallow "guppy breathing" pattern). However, if the patient is deeply sedated and unconscious, it's perfectly acceptable to tolerate this (provided that the ventilator pressures and volumes are within a safe range). The patient may appear outwardly uncomfortable, but if the patient is unconscious, they aren't experiencing it. Paralyzing the patient may alleviate *our* discomfort as providers while making the patient more uncomfortable (by merely masking their discomfort).

[5/6] consider reducing trigger sensitivity on the ventilator

- For a deeply sedated patient, reducing the trigger sensitivity is one way to minimize ventilator-induced lung injury:
  - For an asthmatic patient, tachypnea may drive dynamic hyperventilation.
  - In ARDS, tachypnea may increase mechanical power delivery to the lung.
- Reducing trigger sensitivity may be achieved in various ways, depending on the clinical context. For example, in an asthmatic patient this could be achieved simply by decreasing the PEEP to 5 cm in patients with significant autoPEEP.
- Reducing trigger sensitivity could cause dyspnea and air hunger, so this should only be done in a deeply sedated patient (but by the time you get here, all the patients will be deeply sedated).

[6/6] trial PRN short-term paralytics

- Before committing the patient to a day of paralytic infusion, try a few bolus doses of paralytic (e.g., vecuronium 10 mg IV, repeated up to 2-3 times as needed).
- Many patients only require a few hours of paralysis to facilitate adaptation to mechanical ventilation and allow time to institute the above treatments.
- 💡 If end-tidal capnography is available, pay attention to changes in volumetric CO2 clearance before and after paralysis. A large shift may indicate significant oxygen consumption by skeletal muscles.

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prolonged paralysis

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BIS monitor

- Prior to paralysis, ensure that the patient is well sedated clinically (e.g., sternal rub).
- While paralyzed, monitor sedation using a BIS monitor (a system that monitors cerebral EEG waves to measure arousal).
  - Target a BIS level 40-60.
  - If BIS >60, the patient is too awake – add sedation.

    - If BIS < 40, the patient is over-sedated.
- A similar strategy should be used for any other ICU patient (e.g., multimodal therapy with control of pain, anxiety, and delirium). The target level of arousal is measured using the BIS monitor, but other principles are generally the same.
- One limitation of BIS monitoring is that it may not work well for ketamine (e.g., patient may be entirely dissociated, yet have a relatively high BIS score, suggesting that they are inadequately sedated).

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targeting the appropriate level of paralysis

The ideal level of paralysis and how to achieve this is unknown. To promote ventilator synchrony, 100% total paralysis isn't required.

titrate to the desired clinical efficacy

- The most logical strategy might b*e to* titrate paralytic to the lowest dose that achieves the desired clinical effect. Although there is no high-quality, prospective data supporting this, it would make sense, given that this is how we titrate other medication infusions (e.g., sedatives). (Irwin & Rippe 9e)
- For example, if paralysis is indicated to patient-ventilator synchrony, the lowest dose required to achieve this goal should be utilized (even if that dose *doesn't* cause complete paralysis).

peripheral nerve stimulator (train-of-four)

- Degree of paralysis should be clinically monitored by measuring the number of twitches elicited by sequential stimulation of the muscle with four sequential shocks ("train of four").
    - 0 twitches: excess paralytic.
    - 1-2 twitches: therapeutic paralysis without excessive risk of toxicity.
    - 3-4 twitches: partial paralysis.
    - Even with four twitches, *fading intensity* of subsequent twitches reveals the presence of some paralytic. (32483489 (https://pubmed.ncbi.nlm.nih.gov/32483489/))
- Serial monitoring of the train-of-four may help avoid excessive dosing of paralytics.
- Limitations:
    - Different muscle groups have varying sensitivity.
    - Tissue edema may decrease the current experienced by the patient.

    - Different providers may assess twitches visually or tactilely. (32483489 (https://pubmed.ncbi.nlm.nih.gov/32483489/))
    - Incorrect positioning.
    - ⚠️ Peripheral nerve stimulators alone should not be used as the *sole* tool for paralytic titration.
- Before extubation, train-of-four monitoring may help confirm the *absence* of neuromuscular blockade. (34178382 (https://pubmed.ncbi.nlm.nih.gov/34178382/))

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eye care

- ICUs should have protocols regarding the administration of eye lubrication and eyelid closure.
- Before ICU admission, *gently taping the eyes closed* should prevent dessication or ulceration.

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other risks of paralysis to consider & mitigate

risks/drawbacks of paralytic infusion

- Elevated DVT risk (possibly the strongest independent risk factor among ICU patients). (32483489 (https://pubmed.ncbi.nlm.nih.gov/32483489/))
- Pressure ulceration.
- Nerve injury.
- ICU-acquired weakness (including critical illness neuropathy and/or myopathy).
- Unintended awareness during paralysis.
- Requirement for deep sedation (in efforts to *avoid* awareness). Deep sedation may promote delirium.
- Reduced diaphragmatic activation may reduce recruitment of the lung bases (especially relevant with APRV, which is more effective among non-paralyzed patients).
- Inability to evaluate the patient neurologically. (32483489 (https://pubmed.ncbi.nlm.nih.gov/32483489/))

mitigation of these risks

- Aggressive DVT prophylaxis.

- ICU protocols to avoid pressure injury.
- Close attention to glycemic control may reduce the risk of ICU-acquired weakness.
- Consider avoiding dexamethasone (which may be especially likely to cause myopathy, as compared to other steroids). (33159530 (https://pubmed.ncbi.nlm.nih.gov/33159530/))
- Minimization of paralysis:
  - Wean paralytic infusions to the lowest effective dose.
  - 🏆 Attempt a paralysis vacation at least daily and discontinue paralysis as soon as possible. Short-term paralysis with cisatracurium under close supervision is reasonably safe. However, the odds of developing myopathy increase with each additional day of paralysis. (10378560 (https://www.ncbi.nlm.nih.gov/pubmed/10378560))

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sugammadex

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contraindications, drug interactions, side effects 👎

contraindications

- The only real contraindication is a history of allergy to sugammadex.
- (High-dose sugammadex might cause a slight increase in bleeding; discussed further below).
- (Sugammadex isn't FDA approved for patients with GFR <30 ml/min. However, several studies have reported successful use in this situation without complications – even among patients who are on chronic hemodialysis.) (34178382 (https://pubmed.ncbi.nlm.nih.gov/34178382/) , 32483489 (https://pubmed.ncbi.nlm.nih.gov/32483489/))

drug-drug interactions

- Sugammadex may interfere with toremifene (an estrogen receptor antagonist) and hormonal contraceptives.

side effects

- Risk of allergic/anaphylactic reaction

    - May occur in ~0.3% of patients, even without prior exposure to sugammadex.
    - Anaphylaxis to rocuronium can be treated with sugammadex. However, treatment of anaphylaxis due to sugammadex is more complicated. If the anaphylactic reaction is due to isolated sugammadex, then administration of rocuronium could theoretically be helpful. However, if the anaphylactic reaction is due to the rocuronium-sugammadex complex, then administration of rocuronium could make matters worse (by increasing levels of the rocuronium-sugammadex complex). (41322671 (https://pubmed.ncbi.nlm.nih.gov/41322671/)) For refractory anaphylaxis due to sugammadex following rocuronium induction, if you feel compelled to try something crazy, you could give vecuronium (with the concept that the vecuronium-sugammadex complex may not cross-react with a rocuronium-sugammadex complex). But really, the best therapy is just standard treatment for anaphylaxis with epinephrine.
- Risk of bradycardia and cardiac arrest (if the patient starts developing bradycardia, consider giving epinephrine without delay).
- Alteration in coagulation labs: Sugammadex may cause a transient and small (<25%) increase in PT, aPTT, and TEG R-time. Changes are dose-related and more substantial at doses >4 mg/kg. This doesn't appear to translate into substantially increased clinical bleeding, although FDA labeling does warn about a potential bleeding risk.
- Makes re-intubation challenging. Sugammadex will persist for a while (its half-life is 2 hours and may extend up to 19 hours in severe renal failure). Residual sugammadex may render the administration of aminosteroid paralytic (e.g., rocuronium) *ineffective*. Paralytic options in this scenario include the following:
    - [1] Cisatracurium ⚡ (#cisatracurium_&_atracurium) would be an excellent option (RSI dose is 0.2 mg/kg).
    - [2] Succinylcholine ⚡ (#succinylcholine) may be an option in this scenario (in the absence of contraindications).
    - [3] If the patient received 2-4 mg/kg of sugammadex, this could be overcome by using a very high dose of rocuronium to oversaturate the sugammadex (e.g., 1.5-2 mg/kg). (20630888 (https://pubmed.ncbi.nlm.nih.gov/20630888/)) However, paralysis *will be delayed* for up to several minutes. Therefore, this is *not* a preferred strategy.

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indications, advantages 👍

Sugammadex is a reversal agent for rocuronium or vecuronium (its efficacy against pancuronium is unclear).

how sugammadex should be used

- [1] Sugammadex should *not* be used to reverse rocuronium in critically ill patients with difficult intubation.
- [2] Sugammadex may be utilized to rapidly eliminate rocuronium after RSI, thereby allowing a neurological examination (e.g., in a patient with status epilepticus or traumatic brain injury).
- [3] Paralytic reversal before extubation:
  - [a] Occasional patients are encountered who have bizarrely prolonged paralysis following rocuronium (possibly related to older age or hepatic dysfunction). Sugammadex may be utilized in these patients.
  - [b] Reversal is appropriate for some patients who recently underwent paralysis with rocuronium (discussed in the section below).
- [4] Adjunctive treatment of anaphylaxis due to rocuronium or vecuronium.

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dosing

- Immediate reversal after 1.2 mg/kg rocuronium: 16 mg/kg actual body weight.
- Deep blockade: 4 mg/kg actual body weight.
- Moderate blockade: 2 mg/kg actual body weight.
  - This dose may be adequate when there are ≧2 twitches on a train-of-four. (Paw & Shulman 2025)

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pharmacology

- **Chemical properties**:
  - Molecular weight: 2178 g/mol.
  - LogP: below -6 (*extremely* hydrophilic).
- **Absorption**:
  - Only IV administration.
- **Distribution**:

    - Doesn't bind to proteins.
    - Vd of 11-14 L (0.16-0.2 L/kg). Remains in the extracellular fluid.
- **Metabolism**:
    - Not metabolized.
    - Sugammadex binds to rocuronium extremely tightly and essentially never releases it.
- **Elimination**:
    - >90% is excreted unchanged in the urine.
- **Half-life & duration of action**:
    - The half-life is 2 hours in patients with normal renal function.
    - In severe renal failure, the half-life extends to 19 hours.

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who needs paralytic reversal before extubation?

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It can be challenging to determine which patients would benefit from reversal of rocuronium before extubation. Patients with four twitches on a conventional train-of-four monitoring may be partially paralyzed. Ideally, this would be determined using quantitative train-of-four assessment, but such technology is often absent in medical ICUs.

[1/4] risk factors for persistent paralysis

- Discussed above in the section on rocuronium pharmacology. ⚡ (#aminosteroid_paralytics_(rocuronium,_vecuronium))

[2/4] assessment for residual paralysis

- [1] Train-of-four monitoring:
    - If there are <4 twitches, reversal is definitely needed
    - Assess carefully for *fade* (discussed above). If seen, this would also imply persistent paralytic effects.
- [2] Spontaneous breathing trial:
    - Robust performance on a spontaneous breathing trial suggests that neuromuscular function is adequate for extubation.

- Borderline performance on a spontaneous breathing trial might suggest residual paralytic, atelectasis, or other lingering complications from intubation. Consider paralytic reversal and chest radiograph.

[3/4] final judgment on reversal

- There is no solid evidence to base this on (in the absence of quantitative train-of-four monitoring).
- Practice patterns vary (e.g., some practitioners would reverse all patients who received rocuronium within a few hours, whereas other practitioners would not generally use reversal).

[4/4] choice of reversal agent (if you decide to reverse)

- Sugammadex seems to be the best option (especially for practitioners who aren't facile with dosing neostigmine, which may be tricky).
- There is a small risk of anaphylaxis. If anaphylaxis occurs, it is expected to happen very rapidly after the administration of IV sugammadex.

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paralytic allergy

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- Many paralytics (e.g., atracurium) have the capacity to stimulate histamine release, so there is a potential to misdiagnose histamine release (an anaphylactoid reaction) as a much more dangerous, IgE-mediated *anaphylactic* reaction.
- Anaphylaxic reactions to paralytic agents are a real and problematic phenomenon, however. This seems to be more common in Europe and Australia, possibly related to antigenic exposures which increase cross-allergic responses.
- Sadlier et al. performed one of the most detailed studies evaluating anaphylactic reactions to paralytic agents. In their study, the most common paralytics to cause anaphylaxis were: (23335568 (https://pubmed.ncbi.nlm.nih.gov/23335568/))
    - Rocuronium (56%).
    - Succinylcholine (21%).
    - Vecuronium (11%).
    - Atracurium (9%).

    - No episodes of anaphylaxis due to pancuronium or cisatracurium.
- There appears to be a low risk of cross-allergic reactions between aminosteroid paralytics (rocurinum, vecuronium) and cisatracurium. (23335568 (https://pubmed.ncbi.nlm.nih.gov/23335568/))
- If anaphylaxis occurs following exposure to rocuronium or vecuronium, sugammadex may be used to help treat this. However, the cornerstone of management remains standard therapies for anaphylaxis such as epinephrine (further discussion here: 📖 (https://emcrit.org/ibcc/anaphylaxis/#top)).

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questions & discussion

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To keep this page small and fast, questions & discussion about this post can be found on another page ***here*** (https://emcrit.org/pulmcrit/hyperthermia/) .

Guide to emoji hyperlinks 🔗

- 🧮 = Link to online calculator.
- 💊 = Link to Medscape monograph about a drug.
- 💉 = Link to IBCC section about a drug.
- 📖 = Link to IBCC section covering that topic.
- 🌊 = Link to FOAMed site with related information.
- 📄 = Link to open-access journal article.
- 🎥 = Link to supplemental media.

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